



ANGINA PECTORIS





# MEDICAL TRANSACTIONS,

OF THE  
COLLEGE OF PHYSICIANS  
IN  
LONDON

VOLUME THE SECOND  
THE SECOND EDITION

1787

LONDON  
Printed by J. DODD, at the Sign of the  
Griffin and Dove, in Pall-mall.

## TRANSACTIONS. II

*51. Some Account of a Disorder of  
the Breast. By WILLIAM HENRI  
HARRIS, M. D. F. R. S.*

Read at the COLLEGE, June 21. 1788

**T**HERE is a disorder of the  
breast, marked with strong and  
peculiar symptoms, considerable for  
the kind of danger belonging to it,  
and but extremely rare, of which I  
do not recollect any mention among  
medical authors. The first of it, and  
kind of strangling and anxiety with  
which it is attended, may make it  
not improperly be called *Angina*  
*pectoris*.

Those, who are afflicted with it,  
are tormented, while they are walking,  
and more particularly when they  
walk soon after eating, with a pain-  
ful and great & agreeable sensation  
in the breast, which here & so if it

## II. MEDICAL

would take the little party, if it  
were so minute as to be almost  
the moment they find it, all the  
world is in a flux. In all other oc-  
casions, the patients are, at the begin-  
ning of this disorder, perfectly well,  
and in particular have no sensation of  
breath, from which it is easily dis-  
tinguished.

Access is but continued some  
months, it will not yield to a Pan-  
tology upon standing still, and it  
will come on, not only when they  
are lying down, but when they  
are lying down, and always there  
is a great deal of that kind of anxiety  
for a very short time together, and in  
one or two very severe cases it has  
been brought on by the motion of  
a horse, or a carriage, and even by  
laughter, coughing, going to bed,  
or waking, or by any disturbance  
of the mind. I have heard more, and  
will not pretend, but that he had

SCRIPT OF  
**ANGINA PECTORIS**  
A MOTION PICTURE

WRITTEN AND DIRECTED

BY

**JOSEPH E F RISEMAN, B.S., M.D**

Associate in Medicine Harvard Medical School Instructor in Medicine, Tufts Medical  
School Associate in Medical Research and Associate Visiting Physician  
Beth Israel Hospital, Boston

PHOTOGRAPHED BY

**THE HARVARD FILM SERVICE**

HARVARD UNIVERSITY

A PRODUCTION OF THE  
**BETH ISRAEL HOSPITAL**  
BOSTON MASS

AIDED BY A GRANT FROM  
**BREWER AND COMPANY, INC**  
WORCESTER MASS

COPYRIGHT 1943 BY  
J E F. RISEMAN, B S , M D  
(ALL RIGHTS RESERVED)

FIRST LIMITED EDITION  
PUBLISHED SEPT 1943

PRINTED IN THE  
UNITED STATES OF AMERICA

## FOREWORD

The motion picture Angina Pectoris and this booklet are intended to present, in easily absorbable form, a Clinic on Angina Pectoris. The importance of the clinic method of presenting medical information is of recognized value, but the difficulties of assembling patients and material limits its use. Motion pictures correct some of the difficulties associated with "Dry Clinics," and they have become a valuable method of disseminating medical knowledge. Since a motion picture is portable, it makes a Clinic available to any one, anywhere, any time, it eliminates the difficulties and dangers of assembling patients on time for each presentation, it makes it possible to demonstrate a wealth of material collected, if necessary, from all parts of the globe, furthermore, errors, excess words, illegible charts, etc., can be eliminated in the cutting room. As a result the motion picture method of presenting data is not only interesting but it makes it possible for the observer to absorb a considerable amount of knowledge with a minimum amount of concentration, effort and reading. The finished product may result, however, in such a wealth of material being presented in so short a period of time that the observer is unable to absorb it at one sitting and must either see the picture again or have a means of referring to selected portions of it at his leisure. This illustrated booklet was prepared to supply this need.

It is hoped that the booklet, combined with the motion picture, will aid the student in obtaining a sound understanding of the important facts about Angina Pectoris and will serve as a useful review to those physicians whose busy lives make it impossible for them to read all the publications necessary to obtain this data. The aspects presented are based primarily on work done at the Beth Israel Hospital of Boston. They represent not theories or animal experiments but facts demonstrable by objective studies in patients with angina pectoris.

I wish to acknowledge the valuable assistance of the following who worked without thought of time or remuneration: Dr. Elliot L. Sagall who helped in the preparation of the sets, Mr. James Brewster of the Harvard Film Service for his technical skill and wise counsel, Miss Isabelle Levi for her assistance in preparing the script, and Mr. Howard D. Brewer, president of Brewer & Company, Inc., for his interest in medical research and teaching and whose generous grant made this presentation possible.

JOSEPH E. F. RISEMAN, M. D.  
Boston, Mass.





LIST OF ILLUSTRATIONS .....	13-17
-----------------------------	-------

## PART 1

CLINICAL CHARACTERISTICS OF ANGINA PECTORIS ... ..	23
The Standardized Exercise Tolerance Test . . . . .	24
Color Plates .. . . .	25
The Typical Attack of Angina Pectoris . . . . .	27
Frequency, Physical Build, Age at Onset .. . . .	28
Blood Pressure, Electrocardiogram, Heart Size .. . . .	29
Electrocardiogram During Attacks of Angina Pectoris . . . . .	30
Diagnostic Criteria of Angina Pectoris . . . . .	32

## PART 2

PHYSIOLOGY OF ANGINA PECTORIS . . . . .	35
Studies on Narrowed or Occluded Arteries . . . . .	36
Studies with Induced Anoxia . . . . .	37
Theory of Referred Pain and Angina Pectoris . . . . .	38
Clinical Conditions Associated with Angina Pectoris . . . . .	39
Physiology of Angina Pectoris—Summary . . . . .	40
Color Plates . . . . .	41

	Page
PART 3	
PATHOLOGY OF ANGINA PECTORIS .....	45
Technique—Injection of the Heart ...	46
Color Plates ..	48-49
Technique—Opening the Heart .	51
Technique Concluded ..	52
Characteristic Pathological Patterns	53
Characteristic Pathological Patterns—Summary	54
Color Plates	55
PART 4	
TREATMENT OF ANGINA PECTORIS .	59
Criteria Used to Evaluate Therapy	60
Color Plates	61
Therapeutic Response of Individual Patients	63
Nitroglycerin and other Nitrites .	64
Control Studies—Enteric Coatings	65
Value of Theobromine Sodium Acetate	66
Quinidine Sulfate	67
Sedatives and Analgesics	68
Atropine	70
Color Plates	72-73
Enteric Coated Potassium Iodide	75
Digitalis .	76
Surgery—Frequency of Operation	76
Paravertebral Injection—Thyroid Denervation	77
Total Thyroidectomy	78
Plan for Treatment of Angina Pectoris	79
Treatment—Summary	80

PART 1—CLINICAL CHARACTERISTICS OF ANGINA PECTORIS

	Page
Color Plate 1 Patient B. K. ....	25
Color Plate 2 Patient B. K. During attack of Angina Pectoris (unusually severe or "textbook" type) . . .	25
Color Plate 3 Distribution of Pain in Angina ...	25
Color Plate 4 Clinical criteria diagnostic of Angina Pectoris ..	25
Color Plate 5 Excerpts from electrocardiographic tracing taken continuously during exercise, before, during and after precipitation of Angina Pectoris ..	25
Color Plate 6 Electrocardiogram of normal subject before and immediately after exercise ..	25
Figure 1 Patient R. S. during attack of Angina Pectoris (usual response to attack) ...	23
Figure 2 The two step staircase in the cold room . . .	24
Figure 3 Factors responsible for the variation in ability of patients with angina pectoris to exercise without inducing pain . . .	24
Figure 4 The conditions of the Standardized Exercise Tolerance Test . . .	27
Figure 5 The sex distribution of --- . . .	28
Figure 6 The physical build of --- . . .	28
Figure 7 The age distribution of --- . . .	28
Figure 8 The frequency of hypertension (blood pressure of 160/100 or greater) . . .	29
Figure 9 The frequency of evidence of coronary artery disease in the electrocardiograms of patients with Angina Pectoris . . .	29
Figure 10 The frequency of cardiac enlargement in patients with Angina Pectoris . . .	29
Figure 11 The frequency of patients without hypertension, ab- normal electrocardiograms or cardiac enlargement . . .	30
Figure 12 Method of measuring the heart rate and the blood pressure during exercise . . .	30
Figure 13 Method of recording electrocardiograms during exercise . . .	30
Figure 14 Method of obtaining electrocardiograms during in- duced generalized anoxemia . . .	31

\_\_\_\_\_

## PART 2—PHYSIOLOGY OF ANGINA PECTORIS

		Page
Color Plate 7	Electrocardiograms in clinical and experimental coronary occlusion .....	41
Color Plate 8	Similarity of electrocardiograms in exercise and anoxia .....	41
Color Plate 9	Nerve supply to regions involved by the pain of Angina Pectoris .....	41
Color Plate 10	Diagramatic representation of nerve supply to heart Vagus nerve (Yellow) Cardiac sympathetic nerves (Blue) Thoracic sympathetic nerves (White)	41
Color Plate 11	Diagramatic representation of routes involved (red) in transmission of pain sensation from heart .....	41
Color Plate 12	Schematic representation of discrepancy between the <b>Demand</b> and the <b>Supply</b> of blood during exercise in patients with Angina Pectoris	41
Figure 15	Apparatus used in producing anoxemia in the muscles of the forearm	35
Figure 16	Patient J M with angina pectoris and intermittent claudication on exertion	35
Figure 17	Examination of peripheral circulation in patient J M	36
Figure 18	Sutton and Lueth operation for experimental coronary constriction	36
Figure 19	Apparatus used to induce generalized anoxemia by re-breathing	37
Figure 20	Apparatus used for exercise with oxygen	37
Figure 21	Dissection of cardiac nerves	38
Figure 22	Schematic representation of balance between <b>Supply</b> and <b>Demand</b> with the normal subject at rest	39
Figure 23	Schematic representation of local (cardiac) oxygen debt of normal subject during exercise	40
Figure 24	"The steady state" after several minutes of exercise when the supply of blood equals the immediate needs	40
Figure 25	Recovery from exercise—The supply of blood is greater than the demands until the oxygen debt is cancelled	40

# LIST OF ILLUSTRATIONS

## PART 3—PATHOLOGY OF ANGINA PECTORIS

	Page
Color Plate 13	Parry's book, title page
Color Plate 14	Pig's heart with aorta, pulmonary artery and auncles removed to show the mouths of the coronary arteries . . . . . 48
Color Plate 15	The cannulae tied into the right (red) and left (blue) coronary arteries . . . . . 48
Color Plate 16	Apparatus used in injecting heart by method of Schlesinger . . . . . 48
Color Plate 17	Steps in preparation of injection mass . . . . . 48
Color Plate 18	Washing coronary arteries with saline . . . . . 48
Color Plate 19	Simultaneous injection of right and left coronary arteries . . . . . 49
Color Plate 20	The first incision . . . . . 49
Color Plate 21	The second incision . . . . . 49
Color Plate 22	The third incision . . . . . 49
Color Plate 23	The fourth incision . . . . . 49
Color Plate 24	The fifth incision . . . . . 49
Color Plate 25	The fifth incision completed (viewed from the inside of the heart) . . . . . 55
Color Plate 26	The X-ray, dissected coronary vessels (viewed from the outside of the heart) and diagram of the coronary circulation . . . . . 55
Color Plate 27	The normal circulation (colored X-ray) . . . . . 55
Color Plate 28	Heart of a patient who died of coronary occlusion followed by myocardial infarction . . . . . 55
Color Plate 29	Heart of a patient with Angina Pectoris showing one of the many patterns possible . . . . . 55
Color Plate 30	Heart of a patient with Angina Pectoris showing 9 old complete occlusions . . . . . 55
Figure 26	The first incision completed . . . . . 51
Figure 27	The second incision completed . . . . . 51
Figure 28	The third incision completed . . . . . 52
Figure 29	The fourth incision completed . . . . . 52

# LIST OF ILLUSTRATIONS

## PART 2—PHYSIOLOGY OF ANGINA PECTORIS

	Page
Color Plate 7. Electrocardiograms in clinical and experimental coronary occlusion .....	41
Color Plate 8. Similarity of electrocardiograms in exercise and anoxia .....	41
Color Plate 9. Nerve supply to regions involved by the pain of Angina Pectoris .....	41
Color Plate 10. Diagramatic representation of nerve supply to heart . . . . .	41
Vagus nerve (Yellow)	
Cardiac sympathetic nerves (Blue)	
Thoracic sympathetic nerves (White)	
Color Plate 11. Diagramatic representation of routes involved (red) in transmission of pain sensation from heart . . . . .	41
Color Plate 12. Schematic representation of discrepancy between the <b>Demand</b> and the <b>Supply</b> of blood during exercise in patients with Angina Pectoris	41
Figure 15. Apparatus used in producing anoxemia in the muscles of the forearm . . . . .	35
Figure 16. Patient J M with angina pectoris and intermittent claudication on exertion . . . . .	35
Figure 17. Examination of peripheral circulation in patient J M . . . . .	36
Figure 18. Sutton and Lueth operation for experimental coronary constriction . . . . .	36
Figure 19. Apparatus used to induce generalized anoxemia by re-breathing . . . . .	37
Figure 20. Apparatus used for exercise with oxygen . . . . .	37
Figure 21. Dissection of cardiac nerves . . . . .	38
Figure 22. Schematic representation of balance between <b>Supply</b> and <b>Demand</b> with the normal subject at rest . . . . .	39
Figure 23. Schematic representation of local (cardiac) oxygen debt of normal subject during exercise . . . . .	40
Figure 24. "The steady state" after several minutes of exercise when the supply of blood equals the immediate needs . . . . .	40
Figure 25. Recovery from exercise—The supply of blood is greater than the demands until the oxygen debt is cancelled . . . . .	40

# LIST OF ILLUSTRATIONS

	Page
Figure 10 Duration and degree of effect of nitroglycerin. Comparison of response of Group 1, Group 2, and Group 3 patients . . . . .	63
Figure 11 Frequency of response to nitroglycerin . . . . .	64
Figure 12 Degree of response to nitroglycerin . . . . .	64
Figure 13 Time necessary for disintegration of enteric coated tablets . . . . .	65
Figure 14 Frequency of response to purines . . . . .	66
Figure 15 Degree of response to purines . . . . .	66
Figure 16 Frequency of response to quinidine sulfate . . . . .	67
Figure 17 Degree of response to quinidine sulfate . . . . .	67
Figure 18 Many combinations of sedatives with other drugs are available . . . . .	68
Figure 19 Frequency of response to sedatives . . . . .	68
Figure 20 Degree of response to sedatives . . . . .	68
Figure 41 Frequency of response to cobra venom . . . . .	69
Figure 42 Degree of response to cobra venom . . . . .	69
Figure 43 Frequency of response to atropine sulfate . . . . .	70
Figure 44 Degree of response to atropine sulfate . . . . .	70
Figure 45 As much as 35 drops of the saturated solution of potassium iodide may be necessary to equal 1 c.c. or 1 gram of the drug . . . . .	75
Figure 46 Frequency of response to potassium iodide (3 gm. daily) . . . . .	75
Figure 47 Degree of response to potassium iodide (3 gm. daily) . . . . .	75
Figure 48 Frequency with which surgery was required in patients with Angina Pectoris . . . . .	76
Figure 49 Frequency with which surgery was performed in patients with Angina Pectoris . . . . .	76
Figures 50 and 51 Results of surgery in patient R S . . . . .	77
Figure 52 Results of total thyroidectomy in patients with Angina Pectoris . . . . .	79



PART 4—TREATMENT OF ANGINA PECTORIS

	Page
Color Plate 31	"A tremendous number of methods of treatment have been advocated for Angina Pectoris" 61
Color Plate 32.	The efficacy of over 70 different methods of treatment as evaluated by the Standardized Exercise Tolerance Test and clinical studies . 61
Color Plate 33	Therapeutic agents of great value and the criteria used ... .. 61
Color Plate 34.	Method of disguising medication to prevent recognition by the patient during evaluation studies .... .. 61
Color Plate 35	The frequency with which patients respond to therapy (Groups 1, 2 and 3) .. 61
Color Plate 36	Nitroglycerin prevents the electrocardiographic changes during exercise . . . . 61
Color Plate 37	The most effective Xanthines (uncoated and enteric coated) . . . 72
Color Plate 38	Uncoated and enteric coated purines . 72
Color Plate 39	Comparative degree and duration of effect of Nitroglycerin and Theobromine Sodium Acetate (uncoated and enteric coated) 72
Color Plate 40	Enteric coated potassium iodide . 72
Color Plate 41.	Value of quinidine sulfate in Angina Pectoris 72
Color Plate 42.	The lack of effect of cobra venom on the electrocardiogram during exercise 72
Color Plate 43.	The effect of Digitalis on the electrocardiogram during exercise .... 73
Color Plate 44.	Comparative value of medical and surgical procedures . 73
Color Plate 45	Schematic representation of treatment of Angina Pectoris by decreasing the demand for blood 73
Color Plate 46	Schematic representation of treatment of Angina Pectoris by increasing the coronary blood supply .... .. 73
Color Plate 47	Schematic representation of Angina Pectoris by interrupting the sensory nerves 73
Color Plate 48	The "routine treatment" of Angina Pectoris . 73

# REFERENCES

## PART I

### CLINICAL CHARACTERISTICS OF ANGINA PECTORIS

- Hetherden, W Some Account of a Disorder of the Breast. Med Trans Coll. Phys London, 1768
- Riseman Joseph E F and Stern, Beatrice A Standardized Exercise Tolerance Test for Patients with Angina Pectoris on Exertion Amer Jour Med Sci 188, 646, 1934
- Riseman, Joseph E F and Brown, Morton G An Analysis of the Diagnostic Criteria of Angina Pectoris Amer Ht Jour 14, 331, 1937
- Riseman, Joseph E F The Relation of the Systolic Blood Pressure and Heart Rate to Attacks of Angina Pectoris Precipitated by Effort Amer Ht Jour 12, 53, 1936
- Riseman, Joseph E F, Waller, John V and Brown, Morton G The Electrocardiogram During Attacks of Angina Pectoris Its Characteristics and Diagnostic Significance Amer Ht Jour 19, 683, 1940
- Rothschild, Marcus A and Kissin, Milton Induced General Anoxemia Causing S-T Deviation in the Electrocardiogram Amer Ht Jour 8, 745, 1933
- Levy, Robert L, Barach, Alvan L and Bruenn, Howard G Effects of Induced Oxygen Want in Patients with Cardiac Pain. Amer Ht Jour 15, 187, 1938
- Burrett, C T, Nims, M G and Josephson, C J The Induced Anoxemia Test Amer Ht Jour 23, 306, 1942
- Patterson, James E, Clark, Thomas W and Levy, Robert L A Comparison of Electrocardiographic Changes Observed During The "Anoxemia Test" On Normal Persons and on Patients with Coronary Sclerosis Amer Ht Jour 23 837 1942

## PART 2

### PHYSIOLOGY OF ANGINA PECTORIS

- MacWilliam, J A, and Webster, W J "Some Applications of Physiology to Medicine, Sensory Phenomena Associated with Defective Blood Supply to Working Muscles Brit M J 151, 1923
- Lewis T Pickering, C W and Rothschild, P: "Observations upon Muscular Pain in Intermittent Claudication" Heart 15359, 1931
- Lewis T Pain in Muscular Ischemia Its Relation to Anginal Pain" Arch Int Med 49713 1932
- Sutton D C and Lueth, Harold C Pain Arch. Int Med. 45, 827, 1930
- Blumgart Herrman L Hoff, Hebbel E, Landowne, Milton and Schlesinger, Monroe I Experimental Studies on the Effect of Temporary Occlusion of Coronary Arteries in Producing Persistent Electrocardiographic Changes Amer Jour Med Sci 194, 493, 1937
- Rothschild Marcus A and Kissin Milton Anginal Syndrome Induced by Gradual General Anoxemia Proc Soc Exp Biol Med 29, 577, 1932
- Riseman Joseph E F and Brown, Morton G The Effect of Oxygen on the Exercise Tolerance of Patients with Angina Pectoris Amer Ht Jour 18, 150, 1939
- Head H On Disturbances of Sensation with especial Reference to the Pain of Visceral Disease Brain, 161, 1893 Brain, 17339, 1894 Brain, 19153 1896
- Keefe Chester S and Resnik, William H Angina Pectoris Arch Int Med 41, 769, 1929



Part 1

Clinical Characteristics  
of  
Angina Pectoris

## PART 3

### PATHOLOGY OF ANGINA PECTORIS

- Parry, C H "An Inquiry into the Symptoms and Causes of Syncope Anginosæ Commonly called Angina Pectoris" London 1799
- Schlesinger, Monroe J *An Injection Plus Dissection Study of Coronary Artery Occlusions and Anastomoses* Amer Ht Jour 15, 528, 1938
- Blumgart, Herrman L, Schlesinger, Monroe J and Davis, David *Studies on the Relation of The Clinical Manifestations of Angina Pectoris, Coronary Thrombosis and Myocardial Infarction to the Pathological Findings* Amer Ht Jour 19, 1, 1940

## PART 4

### THERAPY OF ANGINA PECTORIS

- Riseman, Joseph E F *Summary of Ten Years Objective Study of Treatment in Angina Pectoris* New Eng Jour Med (in press)
- Riseman, Joseph E F and Brown, Morton G *Medicinal Treatment of Angina Pectoris* Arch Int Med 60, 100, 1937
- Brown, Morton G and Riseman, Joseph E F *The Comparative Value of Purine Derivatives in the Treatment of Angina Pectoris* Jour Amer Med Assoc 109, 256, 1937
- Riseman, Joseph E F and Brown, Morton G *The Duration of Attacks of Angina Pectoris on Exertion and the Effect of Nitroglycerin and Amyl Nitrite* New Eng Jour Med 217, 470, 1937
- Riseman, Joseph E F and Linenthal, Harry *The Prolonged Use of Enteric-Coated Tablets of Theobromine Sodium Acetate in the Treatment of Edema and Angina Pectoris* New Eng Jour Med 224, 933, 1941
- Freedberg, A Stone, Riseman, Joseph E F and Spiegl, Erwin D *Objective Evidence of the Efficacy of Medicinal Therapy in Angina Pectoris* Amer Ht Jour 22, 494, 1941
- Freedberg, A Stone, Spiegl, Erwin D and Riseman, Joseph E F *Octyl Nitrite in the Treatment of Angina Pectoris* Amer Ht Jour 22, 519, 1941
- Levy, Robert L, Bruenn, Howard G and Williams, Norman E *The Modifying Action of Certain Drugs (Aminophyllin, Nitrites, Digitalis) Upon the Effects of Induced Anoxemia in patients with Coronary Insufficiency* Amer Ht Jour 19, 639, 1940
- Williams, Norman E, Carr, Henry A, Bruenn, Howard G and Levy, Robert L *Further Observations on The Effects of Certain Xanthine Compounds in Cases of Coronary Insufficiency, As Indicated by the Response to Induced Anoxemia* Amer Ht Jour 22, 252, 1941
- Blumgart, Herrman L, Riseman, Joseph E F, Davis, David and Berlin, David D *Therapeutic Effect of Total Ablation of Normal Thyroid on Congestive Heart Failure and Angina Pectoris* Arch Int Med 52, 165, 1933
- Riseman, Joseph E F *The Treatment of Chronic Heart Disease by Total Thyroidectomy* Jour Med Soc New Jersey, July, 1936

# PART I

## CLINICAL CHARACTERISTICS OF ANGINA PECTORIS

In 1768, William Heberden presented before the College of Physicians, in London, a treatise entitled "Some Account of a Disorder of the Breast (Frontispiece) This begins as follows *"There is a disorder of the breast, marked with strong and peculiar symptoms, considerable for the kind of danger belonging to it, and not extremely rare, of which I do not recollect any mention among medical authors. The seat of it, and sense of strangling and anxiety with which it is attended, may make it not improperly be called Angina Pectoris."*

The patient presented in plates 1 and 2 is 65 years of age. She has had angina pectoris for six years. Like most patients with this condition, she is perfectly comfortable between attacks (Plate 1, page 25). On exertion, however, and occasionally on emotion or even while at rest or during sleep, she may develop the characteristic symptoms which we call angina pectoris (Plate 2, page 25).

As will be shown, attacks of angina can be precipitated by having patients repeatedly mount a two-step staircase. During such episodes this patient illustrates dramatically the typical clinical characteristics of this condition.

First—the attacks are obviously uncomfortable (Plate 2, page 25).

Second—the discomfort is located in the anterior chest and inner aspects of the arms.

Third—the attacks are most commonly precipitated by exertion.

Fourth—they are sudden in onset. The pain in this patient did not develop until about 10 seconds before she was forced to stop.

Fifth—the attacks are short in duration.

The attack photographed corresponds closely to the description given in most textbooks, in fact this is the reason that this particular patient was selected. The severity of the pain in this individual and the severity of this patient's reaction to attacks, however, are distinctly unusual. In the attack photographed pain was precipitated by 21 trips over the two step staircase performed in 1 minute and 38 seconds. The attack lasted 1 minute and 42 seconds.

The more common appearance of the attacks as they occur in over 95% of patients is shown in figure 1.



(Figure 1)



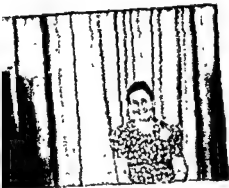


Plate 1—Patient B. K.



Plate 2—"Textbook" attack of angina pectoris



Plate 3—Distribution of pain in angina.

## DIAGNOSTIC CRITERIA

1. Sudden onset
2. Abrupt offset
3. Very discomfort
4. Exercise induces
5. Short duration

Plate 4—Clinical criteria diagnostic of angina pectoris.

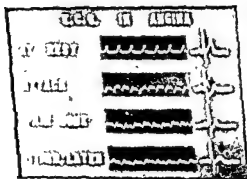


Plate 5—Continuous electrocardiograms during angina on effort

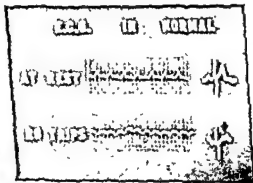


Plate 6—Continuous electrocardiograms of normal during exercise



# THE STANDARDIZED EXERCISE TOLERANCE TEST

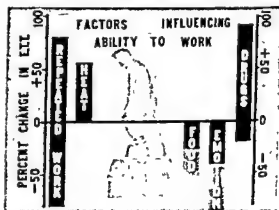
It is important to realize that our knowledge of angina pectoris rests almost entirely upon what patients are able to describe to us about their sensations. Furthermore, so far as we know, this condition exists only in human beings. Therefore, it is necessary to study angina pectoris not in laboratory animals but in patients.



(Figure 2)

The fact that most patients develop attacks on exertion makes it possible to study angina pectoris objectively in the laboratory. Such studies have been carried out since 1932 at the Beth Israel Hospital of Boston. As part of this work, attacks have been precipitated by having the patient exercise in the presence of a physician (fig 2). These studies have been carried out in a room equipped with a refrigerating unit to maintain a constant temperature of 45 to 55 degrees.

This cold room is necessary, for when the various factors influencing the amount of work which can be done before developing an attack were measured, it was soon found that some patients with angina can exercise almost indefinitely at room temperature, whereas, they develop attacks rapidly on exercise in the cold (fig 3). It was also found that a heavy meal will decrease the amount of work which can be done before pain. Excitement or emotion also increases the ease of precipitating attacks. If exercise is repeated or continued, we find that in some patients one attack builds up a slight immunity, while in others the first attack predisposes to a second episode. Similarly, medication may influence the ease of precipitating pain. As a result of these studies, the Standardized Exercise Tolerance Test was developed. This test reproduces in the laboratory the conditions responsible for the majority of attacks in daily life and makes it possible to study angina pectoris objectively without relying on the patient's observations for our basic knowledge.



(Figure 3)

The standardized conditions used in these tests are as follows (fig 4). The temperature of the room is maintained between 45 and 55

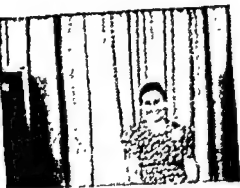


FIGURE 1—PATIENT B. K.



FIGURE 2—"Tartan" attack of anxiety pattern



FIGURE 3—ECG tracing of patient B. K.

## DIAGNOSTIC CRITERIA

1. Sudden onset
2. Anxiety
3. Variable intensity
4. Exaggerated reflexes
5. Short duration

FIGURE 4—Clinical criteria diagnostic of anxiety pattern



FIGURE 5—ECG tracing of patient B. K. showing four leads: I, II, III, and aVR.

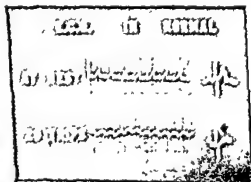


FIGURE 6—ECG tracing of patient B. K. showing four leads: I, II, III, and aVR.

## THE STANDARDIZED EXERCISE TOLERANCE TEST

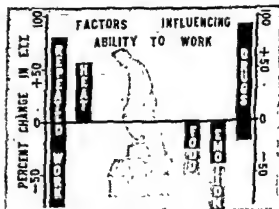
It is important to realize that our knowledge of angina pectoris rests almost entirely upon what patients are able to describe to us about their sensations. Furthermore, so far as we know, this condition exists only in human beings. Therefore, it is necessary to study angina pectoris not in laboratory animals but in patients.



(Figure 2)

The fact that most patients develop attacks on exertion makes it possible to study angina pectoris objectively in the laboratory. Such studies have been carried out since 1932 at the Beth Israel Hospital of Boston. As part of this work, attacks have been precipitated by having the patient exercise in the presence of a physician (fig. 2). These studies have been carried out in a room equipped with a refrigerating unit to maintain a constant temperature of 45 to 55 degrees.

This cold room is necessary, for when the various factors influencing the amount of work which can be done before developing an attack were measured, it was soon found that some patients with angina can exercise almost indefinitely at room temperature, whereas, they develop attacks rapidly on exercise in the cold (fig. 3). It was also found that a heavy meal will decrease the amount of work which can be done before pain. Excitement or emotion also increases the ease of precipitating attacks. If exercise is repeated or continued, we find that in some patients one attack builds up a slight immunity, while in others the first attack predisposes to a second episode. Similarly, medication may influence the ease of precipitating pain. As a result of these studies, the Standardized Exercise Tolerance Test was developed. This test reproduces in the laboratory the conditions responsible for the majority of attacks in daily life and makes it possible to study angina pectoris objectively without relying on the patient's observations for our basic knowledge.



(Figure 3)

The standardized conditions used in these tests are as follows (fig. 4). The temperature of the room is maintained between 45 and 55

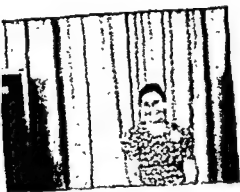


Plate 1—Patient B. K.



Plate 2.—"Textbook" attack of angina pectoris.



Plate 3—Distribution of pain in angina.

## DIAGNOSTIC CRITERIA

1. Sudden onset
2. Anterior chest
3. Variable intensity
4. Exercise induces
5. Short duration

Plate 4—Clinical criteria diagnosis of angina pectoris.



Plate 5—Continuous electrocardiograms during angina on effort.

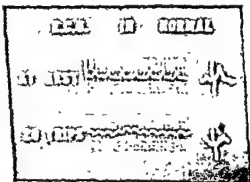
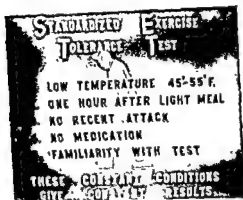


Plate 6—Continuous electrocardiograms of normal during exercise.



## THE TYPICAL ATTACK OF ANGINA PECTORIS



(Figure 4)

degrees Fahrenheit. The exercise is carried out at least one or two hours after a light meal, and the patient rests for one-half hour after coming to the laboratory. No medication is given for at least 12 hours before the test. Only one measurement is carried out on any given day, and no work is performed if the patient has experienced an attack on the way into the hospital, except in those

individuals who always experience many attacks every day. Since excitement frequently induces attacks, it is necessary to minimize the emotional factor; familiarity with the test brings this about.

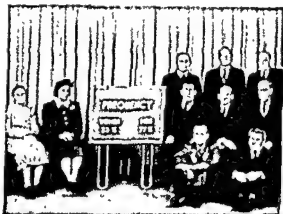
The attack shown in patient R S (fig 1, page 23) does not correspond closely to the usual textbook description but it is absolutely typical of the usual attacks as they occur in daily life in the vast majority of patients. The patient shows no expression of severe discomfort, although he prefers to remain perfectly quiet. There is no fear of impending death and no pallor, flushing, fainting, perspiration or vomiting as has been described by some authors. Although the patient feels that the attack has persisted for some minutes, actual measurement shows that it was about 38 seconds in duration.

The characteristic regions in which patients feel the pain are as follows (Plate 3, page 25). The anterior chest is always involved in an area limited by the anterior axillary lines on the sides, the suprasternal notch above, and the epigastrium below. The region beneath the sternum is the most common location. Radiation of the pain occurs in approximately 60% of patients. The most common region to which the discomfort travels is the left arm, along the inner aspect of the biceps, the elbow, the forearm, the wrist, and the little and ring fingers. In some patients it is referred to similar locations in the right arm. The upper back, in the region of the spine, is commonly involved, although the pain here is not disturbing to the patient. Rarely, it radiates to the neck or to other regions such as the lower jaw.

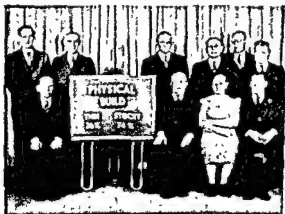
## FREQUENCY, PHYSICAL BUILD, AGE AT ONSET

It has been said that the usual patient with angina is short and stocky, of the so-called vascular build, and that they show abnormalities in the electrocardiogram, blood pressure or heart size. The frequency of the different physical characteristics as actually found in a group of 100 of these patients is as follows

**FREQUENCY** Heberden stated: *"I have seen nearly a hundred people under this disorder, of which number there have been three women."* More recent studies show that it is 3 to 4 times as common in men as in women (fig 5)



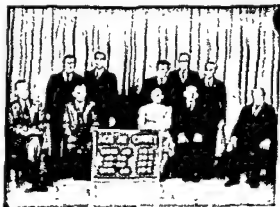
(Figure 5)



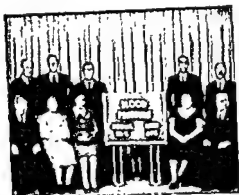
(Figure 6)

**PHYSICAL BUILD** While it is true that the majority of patients are stocky, obese, or "vascular", there are striking exceptions to this rule. It is obvious that the build of the patient is of no aid in establishing the diagnosis (fig 6)

**AGE AT ONSET** Angina pectoris may occur at any age, but it is not common in patients under 40. About 80% of patients are between 45 and 65 years of age when the symptoms first become evident (fig 7)



(Figure 7)



(Figure 8)

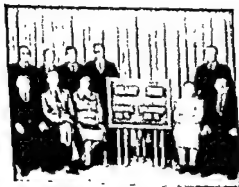
**BLOOD PRESSURE.** Since one-half of the patients have normal blood pressures it is obvious that hypertension is not an important factor in the diagnosis of angina pectoris (fig 8)

#### **ELECTROCARDIOGRAM**

Similarly, only one-half of the patients show evidence of heart disease in the standard electrocardiogram. This is somewhat surprising in view of the fact that these patients all have heart disease, but the heart has many areas which are silent electrocardiographically (fig 9)



(Figure 9)

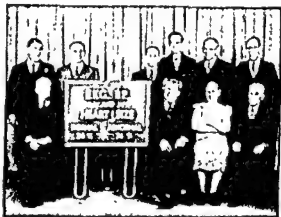


(Figure 10)

**HEART SIZE** Only one-fourth of patients with angina pectoris show cardiac enlargement, even when the measurements are made by X-Ray. This is in sharp contrast to the findings in other forms of heart disease such as congestive failure (fig 10)



ELECTROCARDIOGRAM, BLOOD PRESSURE, and HEART SIZE. One-fourth of the patients with angina show no abnormalities in electrocardiogram, blood pressure or heart size, even though the disease may be advanced and the symptoms severe (fig. 11). It is important to realize that abnormalities in electrocardiogram, blood pressure or heart size are evidence of cardiac damage and are not evidence of heart pain.



(Figure 11)

Since the attacks come suddenly, without warning, and are of short duration, it is obvious that opportunities to make measurements



(Figure 12)

during spontaneous attacks are rare. The heart rate and the systolic blood pressure can be obtained during exercise quite readily by a special technique (fig 12). Such observations show no constant relationship between the heart rate or the height of the blood pressure and the onset or precipitation of the attack.

A few observers have been fortunate enough to obtain electrocardiograms during spontaneous attacks. The short duration of the pain, and the time necessary for the technical procedure of taking such tracings, suggests that these electrocardiograms were obtained toward the end or even after the acute discomfort. The Standardized Exercise Tolerance Test makes it possible to take electrocardiograms continuously before, during and after the attack (fig 13).



(Figure 13)

## ELECTROCARDIOGRAM DURING ATTACKS OF ANGINA PECTORIS

The electrocardiogram taken continuously during the precipitation of an attack practically always shows characteristic changes, especially in the precordial lead. (Plate 5, page 25). These changes begin shortly after the onset of exercise and increase slowly, reaching a maximum at the time when the patient is forced to stop because of pain. The changes consist of a deviation, usually a depression, of the S-T segment as can be seen by comparison with the tracings taken at rest. Thereafter, they either subside rapidly or show further progression, especially in the height of the T waves. While changes in the T waves may occur during the attack, they are more common during recovery from the pain and the exertion.

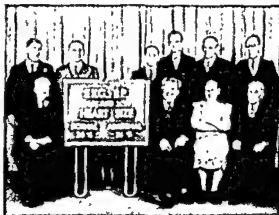
The marked S-T changes found in patients with angina after exertion are not common in normals, but they do occur (Plate 6, page 25). Changes in the T waves, however, are quite frequent. In our experience the electrocardiogram after exercise is of little practical value in the diagnosis of angina pectoris.



(Figure 14)

It has also been found that patients with angina pectoris may show these S-T and T changes when breathing a low concentration of oxygen (figs 14 and 19). Many patients fail to show such changes, however, while an occasional normal individual may show abnormalities which are indistinguishable from those observed in patients with angina. It is obvious, therefore that such changes are of little diagnostic value.

ELECTROCARDIOGRAM, BLOOD PRESSURE, and HEART SIZE. One-fourth of the patients with angina show no abnormalities in electrocardiogram, blood pressure or heart size, even though the disease may be advanced and the symptoms severe (fig 11) It is important to realize that abnormalities in electrocardiogram, blood pressure or heart size are evidence of cardiac damage and are not evidence of heart pain.



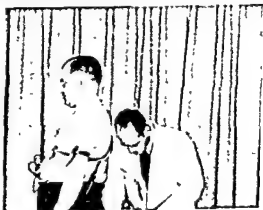
(Figure 11)

Since the attacks come suddenly, without warning, and are of short duration, it is obvious that opportunities to make measurements



(Figure 12)

during spontaneous attacks are rare. The heart rate and the systolic blood pressure can be obtained during exercise quite readily by a special technique (fig 12) Such observations show no constant relationship between the heart rate or the height of the blood pressure and the onset or precipitation of the attack.



(Figure 13)

Part 2

Physiology

of

Angina Pectoris

Obviously, there is little in the physical examination, X-Ray, blood pressure, or electrocardiogram which is of value in the diagnosis of angina pectoris. By observation of patients during attacks, the important diagnostic characteristics were found to be (Plate 4, page 25)

- 1 The attacks are **sudden** in onset with little or no premonitory symptoms.
- 2 The discomfort is in the **anterior** chest. Radiation of the pain is important if it occurs, but it may be absent.
3. The discomfort is **vague** in character and difficult for the patient to describe.
- 4 **Exertion** is the most common precipitating cause, although it may also occur on emotion.
- 5 The attacks are **short** in duration. According to the patient they rarely last longer than 15 to 20 minutes.

Practically all patients show all five clinical characteristics. Difficulties in diagnosis arise mainly because of the inability to obtain a clear cut description of the patient's symptoms. Under such conditions, observation of the patient during a typical attack may be of considerable value in diagnosis.

Heberden's classic description includes the five characteristics which recent experience has shown to be of diagnostic value (frontispiece)

*"Those, who are afflicted with it, are seized, while they are walking, and more particularly when they walk soon after eating, with a painful and most disagreeable sensation in the breast, which seems as if it would take their life away, if it were to increase or to continue: the moment they stand still, all this uneasiness vanishes."*

## PART 2

### PHYSIOLOGY OF ANGINA PECTORIS

There is considerable evidence in the literature that attacks of angina pectoris occur when the heart muscle receives an insufficient amount of oxygen or blood or both. This anoxemia or ischemia theory is consistent with more of the known clinical facts concerning angina pectoris than is any other concept. Furthermore, it makes many characteristics of the disease more understandable. There is considerable experimental evidence in favor of this theory.

Lewis showed that muscular exercise, in the absence of an adequate blood supply, causes pain in the muscles used. We can occlude the blood supply to the arm of a normal healthy subject by inflating a blood pressure cuff to a level greater than that of his arterial blood pressure (fig 15). If the muscles of the forearm are then exercised, the available oxygen dissolved in the tissues is soon used up, and the subject experiences first fatigue, then pain in those muscles involved. This pain rapidly increases in severity and continues even though exercise is stopped. As soon as the tourniquet is released however, fresh blood enters the arm and the pain disappears immediately.



(Figure 15)



(Figure 16)

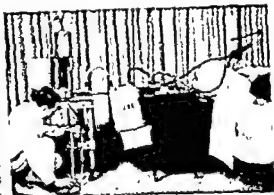
The clinical counterpart of this experiment is seen in patients who have arteriosclerosis involving the arteries of the heart and also those of the legs. On exercise, such patients may develop not only angina pectoris but also pain in the calf muscles (fig 16). This condition called 'intermittent claudication' is fairly common among elderly individuals even in the absence of angina pectoris.



## STUDIES WITH INDUCED ANOXIA

changes are associated with an insufficient supply of oxygen to the heart muscle. Their occurrence may be of value in establishing the diagnosis of myocardial infarction.

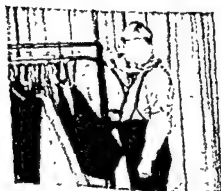
Another line of evidence in favor of the anoxemia theory was presented by Rothschild and Kissin in 1932 who showed that attacks of angina pectoris could be precipitated in some patients at rest by having them breathe low concentrations of oxygen (fig 19). The apparatus consists of a spirometer, such as an ordinary basal metabolism machine, connected in series with a reservoir of about 20 liters,



(Figure 19)

and a motor blower to insure circulation. As a result of this re-breathing, the oxygen content, as determined by analysis, is decreased to as low as 8 or 10%. Under these conditions, some but not all patients with angina develop pain.

Electrocardiograms taken during such experiments (Plate 8, page 41) may show changes in the S-T segment and the T wave identical with those observed in the same patient during spontaneous attacks of angina or during attacks induced by exercise. These changes are similar to those found in some patients with coronary occlusion. Such studies indicate that attacks of angina are associated with myocardial anoxia regardless of whether they are produced spontaneously, by exercise, or by generalized anoxemia.



(Figure 20)

The opposite of this type of experiment has been performed by Riseman and Brown in 1939 (fig 20). Their investigations show that exercise while breathing pure oxygen enables patients with angina to do more work without pain than is possible under the usual standardized conditions, even though handicapped by the apparatus.



The presence of arteriosclerosis in the legs is indicated by the absence of palpable pulsations of the dorsalis-pedis and the posterior-tibial arteries and also by the relatively cold temperature of the feet. This can be demonstrated by the sense of touch. More accurate measurements with a dermaterm show that the temperature



(Figure 17)

of the great toe is considerably less than that of other parts of the body, such as the thumb (fig 17)



(Figure 18)

In 1930, Sutton and Lueth showed experimentally the relationship of anginal pain to narrowing of the coronary arteries. In these experiments an animal was anesthetized, the heart was exposed, and a ligature passed about one of the coronary arteries (fig 18). After recovering from this operation, they could occlude the artery at will by gentle traction. This

constriction caused discomfort in the chest and left paw.

The clinical condition "coronary occlusion" simulates this experiment. In this condition patients suddenly develop pain in the chest which is similar to their anginal attacks but is much more severe and continues for several hours. Post-mortem examination of such individuals usually reveals that one of the major arteries of the heart has become completely occluded so that the cardiac circulation is restricted similarly to the artificial restriction in the experimental animal (see part 3).

Electrocardiograms taken during experimental coronary occlusion in dogs or coronary thrombosis in man (Plate 7, page 41) may show S-T segment and T wave changes similar in character but more pronounced than those seen in attacks of angina pectoris. These

quate blood flow, or regurgitation of such a degree that during diastole a portion of blood flows back into the heart rather than through the coronary vessels

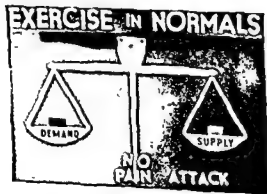
Abnormal rhythms, especially if the rate is rapid, may result in poor circulation. Under such conditions, the increased work of the heart together with the poor blood flow, may result in myocardial anoxia and angina pectoris

In anemia, the decreased number of red blood corpuscles results in a decreased supply of oxygen to the heart. In addition, the heart has to work harder to supply the necessary oxygen. As a result, many elderly patients with anemia experience heart pain.

In exophthalmic goiter, the tissues of the body, including the heart, require an increased amount of oxygen and the heart beats faster. As a result, a few patients develop angina.

Similarly, some patients with congestive failure, although complaining primarily of dyspnea, may experience a feeling of pressure, choking, squeezing or pain in the anterior chest or arms.

Patients with emphysema or asthma also complain of symptoms simulating angina pectoris. In these individuals the abnormality of the lungs prevents adequate oxygenation of blood when the patient exercises.



The mechanism of angina pectoris can be summarized and illustrated by the Law of Supply and Demand as it applies to the coronary circulation.

In the normal individual and in most patients with angina pectoris the Supply of blood through the coronary vessels is adequate for

the needs or Demands of the myocardium when the subject is at rest (fig. 22)

The theory of referred pain as presented by Head in 1893 explains why patients, who exercise with their legs, experience pain in the anterior chest and inner aspects of the arms

The usual distribution of pain in angina pectoris (Plate 9, page 41) is innervated, in the chest, by the eighth cervical, the first second, third, fourth, and fifth thoracic nerves. The sensory innervation of the inner aspect of the arm is derived from the eighth cervical, the first and second thoracic nerves

The anatomic nerve supply to the heart is well known. An actual dissection of these nerves shows that it is a most complex network (fig 21). The cardiac nerve supply consists of fibers from the vagus, which unite with the cervical sympathetic, and the thoracic sympathetic chain and ganglia (plate 10, page 41). Functionally, the sympathetic nerves connect



(Figure 21)

with the ganglia of the eighth cervical, the first, second, third, fourth and fifth thoracic nerves. Impulses which arise in the heart travel up the sympathetic nerves to the nerve roots in the dorsal ganglia and spinal cord. The sensation of pain set up by these impulses is felt not in the organ actually involved, but in the areas innervated by the peripheral nerves arising in the same segments of the spinal cord (Plate 11, page 41).

Thus, the sensations set up in the heart by anoxemia are experienced as pain in the anterior chest and inner aspects of the arms

The anoxemia-ischemia theory helps considerably in understanding why angina pectoris is associated with certain diseases

For example, it is most commonly found in elderly individuals of the arteriosclerosis age group

Syphilis of the aorta and mouths of the coronary arteries may also be a cause of inadequate coronary circulation

Similarly, some patients with disease of the aortic valves may complain of angina pectoris. In these patients, examination of the valves may reveal a degree of stenosis so great as to prevent an ade-

## CLINICAL CONDITIONS ASSOCIATED WITH ANGINA PECTORIS

quate blood flow, or regurgitation of such a degree that during diastole a portion of blood flows back into the heart rather than through the coronary vessels.

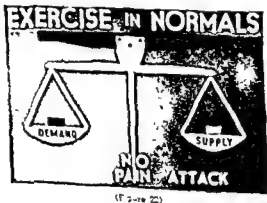
Abnormal rhythms, especially if the rate is rapid, may result in poor circulation. Under such conditions, the increased work of the heart together with the poor blood flow, may result in myocardial anoxia and angina pectoris.

In anemia, the decreased number of red blood corpuscles results in a decreased supply of oxygen to the heart. In addition, the heart has to work harder to supply the necessary oxygen. As a result, many elderly patients with anemia experience heart pain.

In exophthalmic goiter, the tissues of the body, including the heart, require an increased amount of oxygen and the heart beats faster. As a result, a few patients develop angina.

Similarly, some patients with congestive failure, although complaining primarily of dyspnea, may experience a feeling of pressure, choking, squeezing or pain in the anterior chest or arms.

Patients with emphysema or asthma also complain of symptoms simulating angina pectoris. In these individuals the abnormality of the lungs prevents adequate oxygenation of blood when the patient exercises.

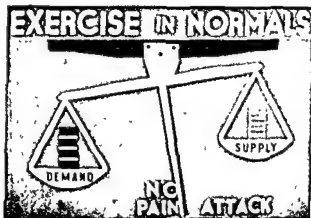


The mechanism of angina pectoris can be summarized and illustrated by the Law of Supply and Demand as it applies to the coronary circulation.

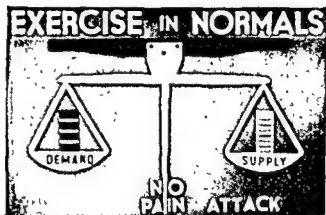
In the normal individual and in most patients with angina pectoris the Supply of blood through the coronary vessels is adequate for

the needs or Demands of the myocardium when the subject is at rest (Fig. 2-21).

On exercise, however, the heart must work harder and, therefore, the **Demands** of the myocardium increase. In response to this increased demand, the **Supply** of blood through the coronary arteries also increases, but lags behind (fig 23). As a result, a slight relative anoxia of the myocardium exists for



(Figure 23)

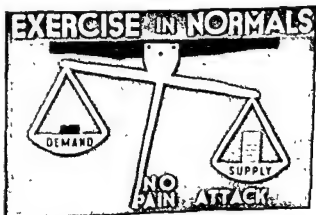


(Figure 24)

several minutes until the balance is re-established (fig 24)

With cessation of work, the opposite takes place. The **Demand** is decreased to the resting level, and the coronary blood **Supply** soon decreases also to a degree sufficient for the body at rest (figs 25 and 22).

The situation is quite different in angina pectoris. Here, when the **Demands** are increased by exercise, the coronary circulation is not able to increase (Plate 12, page 41). This discrepancy between the **Demands** for blood and the **Supply** of blood causes marked myocardial anoxia and ischemia. As a result, the patient experiences heart pain. This is referred to the chest and arms



(Figure 25)

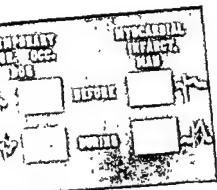


Plate 7—Electrocardiograms in coronary occlusion

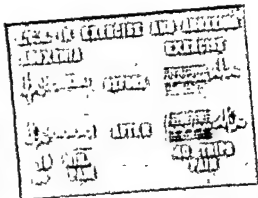


Plate 8—Similarity of electrocardiograms in exercise and anoxia



Plate 9—Sensory nerve distribution in angina pectoris



Plate 10—The cardiac nerves





Part 3  
Pathology  
of  
Angina Pectoris





## PART 3

### PATHOLOGY OF ANGINA PECTORIS

Parry's Book on angina pectoris published in 1799, includes a transcript of a letter from Dr Jenner. This reads in part as follows (Plate 13, page 48) *"I was making a transverse section of the heart pretty near its base when my knife struck against something so hard and gritty as to notch it. I well remember looking up to the ceiling which was old and crumbling, conceiving that some planter had fallen down. But on a further scrutiny the real cause appeared, the coronaries were become bony canals"* Recent work on the anatomy and pathology of the heart has confirmed the findings of Jenner

The coronary circulation is not easy to see in the gross specimen. It consists of the left coronary artery which divides into the left anterior descending branch and the left circumflex branch. There is also a right coronary artery. If we remove the aorta, pulmonary artery and the auricles we can see the mouths of these vessels coming off the aorta just at the base of the cusps of the aortic valves (Plate 14, page 48)

The simplest method of studying the coronary arteries is to open the lumen of each vessel with a fine pointed scissors. The objections to this method are that it may dislodge fresh occlusion and, furthermore, it is not suitable for studying vessels smaller than 1 millimeter in diameter

According to a second method, the vessels are cut across at frequent intervals and then probed. This has the same drawbacks as the previous method.

Hearts have been injected with various radio-opaque materials and studied by X-Ray. The vessels appear to cross each other, however, and adequate study is difficult

A simple practical method which corrects these difficulties was devised by Schlesinger in 1939. This method combines the use of Injection, X-Ray, and Dissection. By means of it we can study the entire course of each blood vessel down to 40 micra. Areas of obstruction or narrowing too small to be seen by other methods of study are readily observed, and the presence of anastomotic circulation is easily recognized. This method has given us considerable information about the pathology of angina pectoris. The method can be used in the routine examination of all post-mortem material. The technique is simple

## TECHNIQUE—INJECTION OF THE HEART

---

Glass cannulae, connected to short lengths of rubber tubing and metal adapters, are carefully inserted into the mouths of the coronary arteries and tied into place securely (Plate 15, page 48)

A bath of warm isotonic saline is prepared by mixing one part of 18% salt solution with 19 parts of hot tap water (Plate 16, page 48) A heating unit and thermostat adjusts the temperature of this bath to 45 degrees centigrade The heart is suspended in the bath, and a thermometer is inserted into one ventricle

While the heart is being warmed, the injection mass can be prepared (Plate 17, page 48). One and one-half grams of agar-agar are weighed out, using an ordinary balance This is placed in a pyrex container which can be covered To this is added 100 cubic centimeters of a 30 per cent solution of lead acetate in water 70 cubic centimeters of a 12 per cent solution of anhydrous sodium phosphate is added and mixed by shaking. This results in the precipitation of the insoluble and radio-opaque lead phosphate Phenolsulfonphthalein is added as an indicator With a graduated pipette, enough ten percent sodium hydroxide is added, with shaking, to neutralize until the first pink color appears Finally, distilled water is added to bring the total volume up to 200 cc Usually, 10 to 20 cubic centimeters are required The agar-agar is brought into solution by heating over an open flame Boiling is continued for 10 minutes The mixture froths vigorously, and frequent shaking is necessary to prevent its boiling over The hot injection mass is then filtered through a double layer of gauze into narrow mouthed 50 c c centrifuge tubes Finally, the injection mass is colored by the addition of dyes fuchsin is added to give a red color and methylene blue for blue The tubes are stoppered and shaken thoroughly to ensure mixing

A flask weighted with lead is filled with saline from the bath The injection mass is kept warm to prevent solidification of the agar Both cannulated arteries are connected to the flask which in turn is connected to a mercury manometer With a cautery bulb the pressure in the system is raised to 200 millimeters of mercury This forces saline into the arteries and removes the residual air and blood (Plate 18, page 48)

The containers of colored, radio-opaque mass are now fitted with two hole rubber stoppers so that pressure can be applied above the fluid and the mass forced out The containers are connected to the



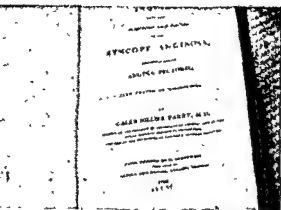


Plate 13—Syncope Anginosa-Parry



Plate 14—The mouths of the coronary arteries



Plate 15—The cannulae in the coronary arteries

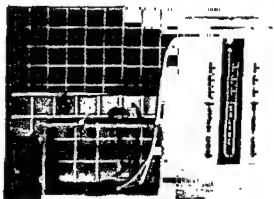


Plate 16—Apparatus for injecting hearts

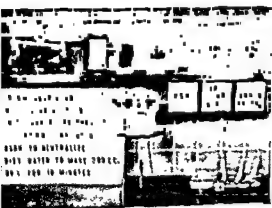


Plate 17—Preparation of injection mass.

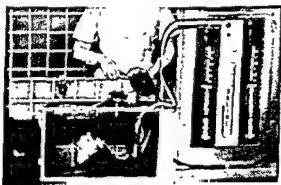


Plate 18—Washing coronary arteries with saline



Figure 19—Injecting the coronary arteries



Figure 20—The first incision.



Figure 21—The second incision

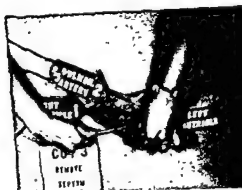
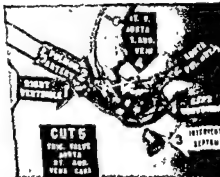


Figure 22—The third incision





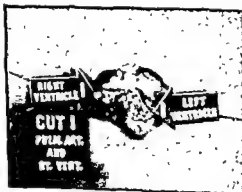
manometers, and also to the heart in such a way that the blue mass can be injected into the left coronary and the red mass into the right (Plate 19, page 49) The manometers are joined so that the pressure is the same throughout the system

The valve to the saline is shut off and the valves to the arteries turned on The pressure in the system is raised to 200 millimeters of mercury This injects the mass into both arteries simultaneously at identical pressure The red mixture fills the right coronary artery, the blue mass fills the left

The cannulae are then clamped off, and in order to harden the agar-agar injection mass the heart is placed in a bath of ice and salt solution for about 10 minutes

The injected heart is then unrolled by a series of incisions, so that the vessels lie in one plane

The first incision starts in the pulmonary artery and divides the pulmonary valve (Plate 20, page 49) It also cuts the right ventricle to the apex just to the right of the interventricular septum This results in the opened right ventricle lying to your left,

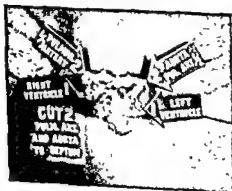


(Figure 26)

while the left ventricle remains intact (fig 26)

The second incision starts in the aorta between the two cannulated vessels and extends into the base of the interventricular septum (Plate 21, page 49) This again divides the pulmonary artery (fig 27)

The interventricular septum is now removed in one piece as close as possible to the walls of the left ventricle

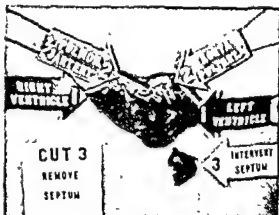


(Figure 27)

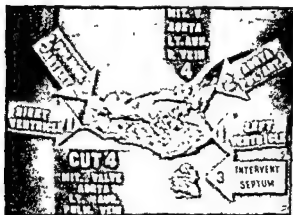


(Plate 22, page 49). A scalpel is best for this procedure. This partially opens the left ventricle (fig. 28).

The fourth incision starts in one of the pulmonary veins. It cuts the aortic ring and the anterior cusp of the mitral valve (Plate 23, page 49). This unrolls the left ventricle. (fig 29)



(Figure 28)



(Figure 29)

The fifth and final incision goes through the su-vena cava, the aortic ring again and the tricuspid valve (Plate 24, page 49). This permits the right ventricle to be unrolled completely (Plate 25, page 55)

The heart has now been opened without having cut any of the major vessels. Furthermore, all the vessels now lie in one plane. An X-ray of the unrolled heart is now taken. Using the X-ray as a guide, the vessels are carefully dissected. By studying the X-ray together with the dissection, tiny areas of narrowing and obstruction not recognizable by other methods of study can be detected readily.

From the X-ray and the dissection, a colored diagram is made. This diagram, together with the X-ray, are permanent records (Plate 26, page 55). The myocardial tissue can be examined microscopically and then discarded.

## CHARACTERISTIC PATHOLOGICAL PATTERNS

From a careful study of the X-ray, the dissection and the diagram, the course of the coronary circulation during life can be visualized

### THE NORMAL CIRCULATION

Plate 27, page 55, shows a normal heart obtained from a man 63 years of age with no cardiac disease who died of intestinal obstruction following operation. In the normal heart, the injection mass flows smoothly through the entire length of the blood vessels both left and right. There is no obstruction, delay, or any evidence of collateral or anastomotic circulation. This normal pattern is quite different from those seen in coronary artery disease.

### MYOCARDIAL INFARCTION

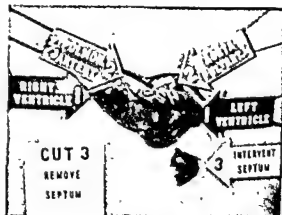
The heart shown in plate 28, page 55, was obtained from a man 50 years of age with angina for only 11 days before the onset of myocardial infarction which resulted in death. The left anterior descending artery shows an area of narrowing but no obstruction near its origin. The left circumflex shows a similar area of arteriosclerosis with a thrombus completely occluding its lumen. The right coronary artery and distal portion of the left descending are normal. The left circumflex, however, fills poorly beyond the occlusion. There are no adequate anastomoses. As a result, the circulation was unable to compensate for the sudden occlusion of the left circumflex artery. An infarct developed in the area nourished by this vessel, and the patient died of a ruptured myocardium.

### ANGINA PECTORIS—One Pattern

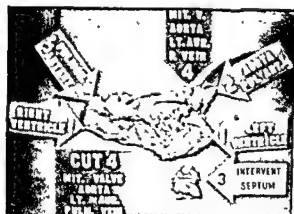
A third heart (Plate 29, page 55) was obtained from a woman 60 years of age who had angina pectoris for 5 years. At post mortem it showed one of the many patterns possible in this condition. There was an old complete occlusion of the right coronary artery near its mouth. This prevented the red mass from going further. There was marked arteriosclerosis of the left circumflex and left descending arteries resulting in narrowed tortuous lumens, and there was a second old occlusion in the left descending artery. In response to these narrowings and occlusions a rich anastomotic network was built up during life so that the circulation to the right side of the heart was maintained from the left coronary artery. This anastomotic circulation was adequate to maintain life for several years despite occlusions of two of the main coronary arteries. The coronary circulation was impaired, however, so that the myocardium suffered from ischemia, and the patient experienced angina pectoris.

(Plate 22, page 49). A scalpel is best for this procedure. This partially opens the left ventricle (fig. 28).

The fourth incision starts in one of the pulmonary veins. It cuts the aortic ring and the anterior cusp of the mitral valve (Plate 23, page 49). This unrolls the left ventricle (fig. 29).



(Figure 28)



(Figure 29)

The fifth and final incision goes through the su-vena cava, the aortic ring again and the tricuspid valve (Plate 24, page 49). This permits the right ventricle to be unrolled completely (Plate 25, page 55).

The heart has now been opened without having cut any of the major vessels. Furthermore, all the vessels now lie in one plane. An X-ray of the unrolled heart is now taken. Using the X-ray as a guide, the vessels are carefully dissected. By studying the X-ray together with the dissection, tiny areas of narrowing and obstruction not recognizable by other methods of study can be detected readily.

From the X-ray and the dissection, a colored diagram is made. This diagram, together with the X-ray, are permanent records (Plate 26, page 55). The myocardial tissue can be examined microscopically and then discarded.



25—The L<sub>1</sub>/2 incision completed.

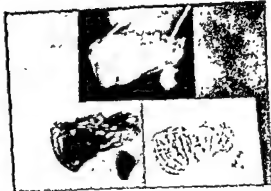


Plate 26—The complete preparation.



Plate 27—Normal circulation.

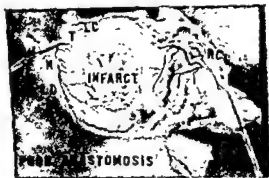


Plate 28—Myocardial infarction.

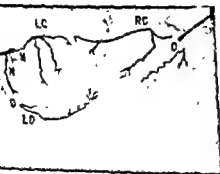


Plate 29—Angina pectoris.



Plate 30—Angina pectoris.

**ANGINA PECTORIS—Many Old Occlusions**

A fourth heart (Plate 30, page 55) obtained from a man 53 years of age, shows how extensive occlusions and anastomoses can be. The left circumflex artery had an old occlusion near its mouth. The first branches of the right coronary and the left descending arteries were also occluded. There was an old occlusion of the left descending artery and also of its second major branch. A fresh thrombus, the cause of death, was found in the right coronary artery and there was an old occlusion near this point. Anastomoses had developed beyond these occlusions so that the branches received blood from the major vessels. A seventh occlusion failed to stop the circulation. The flow of blood must have been reversed in some of the terminal branches, for they received blood from the opposite sides of the heart. An eighth occlusion, in a branch of the left descending also caused reversal of the flow of blood. *A ninth occlusion was found in another terminal branch.* The remainder of the vessels were filled by mass from both the right and left coronary arteries. Despite these 9 old occlusions, this patient with angina pectoris was active in business up to 22 hours before death. There was only one, small, old infarction.

An analysis of the variations in the circulatory pattern found in coronary artery disease shows the following

First, complete occlusion of one or more of the major vessels is a common occurrence

Second, these occlusions do not prevent longevity and physical activity, providing an adequate collateral circulation develops

Third, angina pectoris occurs when following coronary occlusion the collateral circulation is not adequate to Supply the Demands of the myocardium during exercise

Part 4

Treatment

of

Angina Pectoris



## PART 4

### TREATMENT OF ANGINA PECTORIS

A tremendous number of methods of treatment have been advocated for angina pectoris (Plate 31, page 61) According to the published reports, each of these methods makes the patient more comfortable Little exact or comparative information of their effect has been available, however

Since, so far as we know, angina pectoris exists only in humans the benefits of therapy must be evaluated not in laboratory animals but in patients.

The value of any method of treatment can be measured objectively by the Standardized Exercise Tolerance Test For example, the value of nitroglycerin can be demonstrated as follows The amount of work which a patient can do without medication before developing pain is found by repeated tests under the usual standardized conditions of cold, food, and so forth which have been found to give constant results The patient then places a tablet under his tongue and waits a measured length of time for it to take effect The test is then repeated By means of a counter and stop-watch, we again measure the amount of work which he can do By this method we can demonstrate that most patients after nitroglycerin can do more work, without pain, than was possible without medication

Obviously, since most patients with angina develop their attacks on exertion, any treatment of value must enable the patient to perform more work before developing pain This objective method of study makes it possible to evaluate the effect of treatment without being influenced by the impression of the patient or the physician

This objective method of study has been used in the Angina Clinic of the Beth Israel Hospital of Boston since 1932, the results have proven of value in the clinical management of patients Up to the present time the efficacy of over 70 different methods of treatment have been tested and compared (Plate 32, page 61)

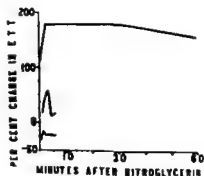
A group of about 20 methods have been found of great value, others have been of slight or only moderate value, while despite the claims of the manufacturers, many are of little value





## THE NITRITES

Generations of patients and doctors can testify to the value of nitroglycerin for decreasing the length of attacks. It is also helpful in preventing attacks. For example, studies in one patient (fig 30, center curve) showed him able to do 20 per cent more work if exercise is started 1 minute after nitroglycerin. After 2 minutes he can do 40 per cent more work. After 3 minutes, 60 per cent more. Shortly after this, however, the effect diminishes rapidly and disappears within 10 minutes. Experience shows that this is a moderate response to nitroglycerin.



(Figure 30)

Other patients show far more striking benefit. They can do at least 100 per cent more work for at least one half hour after taking nitroglycerin (fig 30, top curve). A third group of patients show no response to this therapy (fig 30, bottom curve).

The response to nitroglycerin can be used to determine the probability of a patient's response to other forms of treatment (Plate 35, page 61).

For example, one group of patients is able to perform approximately 100 per cent more work when given nitroglycerin. When given other drugs, they show a definite increase in exercise tolerance and, more important, practically complete disappearance of attacks in daily life. This group consists of a little less than one-third of the patients.

A second group is able to do approximately 50 per cent more work after nitroglycerin. When these patients are given other medication they show a definite decrease in frequency of attacks in daily life but attacks are not likely to disappear entirely. This group includes one third of the patients.

A third group is unfortunate for they show no response to nitroglycerin or any of the usual methods of treatment. This group includes 40 per cent of patients.

It is thus possible to divide patients with angina pectoris into three groups on the basis of their response to therapy.

That these results are due to actual changes in the heart and not to psychological influence can be shown by taking electrocardiograms during and following exercise (Plate 36, page 61). Under ordi-



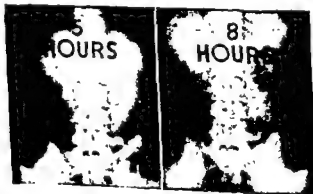
## THE PURINES

According to animal experiments and electrocardiographic studies in patients, these drugs are vasodilators. Theobromine and theophylline which are obtained from cocoa or tea are relatively insoluble. They can, however, be joined with many other substances to form loose chemical combinations which increase their solubility and effectiveness. Many of these have been prepared and are available for use. The comparative value of 18 different xanthine derivatives have been measured and demonstrated by the Standardized Exercise Tolerance Test. A few are of considerable value. Many widely advertised brands, however, are of little value.

In order to control these studies, and to eliminate the psychological factor, the response has been compared to that obtained following sodium bicarbonate or lactose prepared to resemble the medication being studied (Plate 34, page 61). The response to medication when disguised by dipping in tincture cudbear served as an additional control. Electrocardiographic studies further differentiate between active and inert therapy.

The most effective of these xanthines are Theobromine Sodium Acetate, Theophylline Sodium Acetate, and Theophylline Calcium Salicylate (Plate 37, page 72).

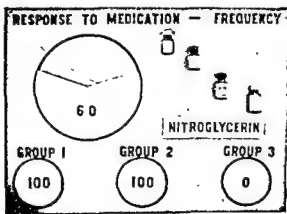
All the xanthines when given in sufficient dosage cause gastric distress but this can be prevented by encasing them in an enteric coating which enables them to pass through the stomach intact and disintegrate in the small intestine (Plate 39, page 72). In most patients absorption takes place in 4 to 6 hours (fig 33). It must be remembered therefore, that it is the tablet given before retiring which is effective in the early morning.



(Figure 33)

nary conditions, the patient illustrated shows definite changes in the S-T segment of the electrocardiogram at the time when an attack is precipitated by exercise. When nitroglycerin or other effective vasodilators are given, the patient can perform a greater amount of work than is otherwise possible. At the same time, the electrocardiographic changes ordinarily observed either do not occur or are markedly diminished.

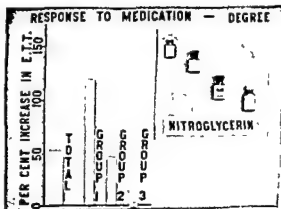
Nitroglycerin can be absorbed readily by the mucous membrane under the tongue. Since the duration of attacks is short, the medication must be absorbed within a period of a few seconds. For this reason, the more soluble hypodermic tablets are preferable to tablet triturates. A properly prepared tablet should dissolve in water at room temperature in about 1 minute. The toxic or untoward effects of nitroglycerin are seen more commonly in young individuals than in those with arteriosclerosis. They are due to vasodilation and consist of a burning and flushing of the face, together with headache, and occasionally faintness, if there is a marked fall in blood pressure. In most instances 1/200 grain of nitroglycerin is as effective as larger doses and is less likely to give untoward effects.



(Figure 31)

Amyl Nitrite can be used by inhalation. It is an effective nitrite but offers no particular advantage over nitroglycerin and is more costly. The same is true of Octyl Nitrite which also is given by inhalation. Erythol-tetranitrate and Mannitol Hexanitrate are considerably less effective. Sodium Nitrite is of little or no value.

Nitroglycerin is one of our most valuable drugs (figs 31, 32). It is clinically effective in 60 per cent of patients (Groups 1 and 2). It is of low toxicity and low in cost. Its use before work results in an average increase in exercise tolerance of about 120 per cent in patients of Group 1. The optimum dose is 1/200 grain, but 1/400 every hour is of considerable value in some patients.



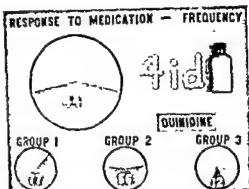
(Figure 32)

## QUINIDINE SULFATE

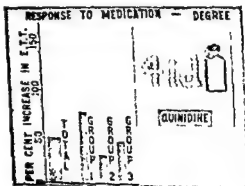
### QUINIDINE SULFATE

Quinidine has not been used sufficiently in angina pectoris. Experience in over 100 patients has shown that this drug is clinically effective, low in toxicity in patients with angina, and low in cost. The administration of the sulfate in doses of 5 grains four times a day helps approximately 44 per cent of patients (figs 36-37). What is more important is that it is often of

value in patients not benefited by the xanthines. Its use results in an increase in exercise tolerance of about 50 per cent.



(Figure 35)



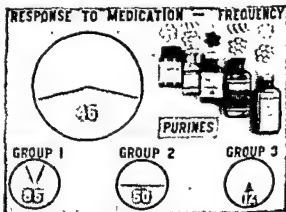
(Figure 37)

Objective evidence of the value of quinidine can be obtained from the study of the electrocardiogram during work (Plate 41, page 72). After quinidine is given, exercise fails to induce the S-T segment changes usually seen when no medication is administered. Quinidine also causes a prolongation of the Q-T interval (the duration from the beginning of the QRS to the end of T). This specific effect shows that quinidine acts for about 6 hours after administration.

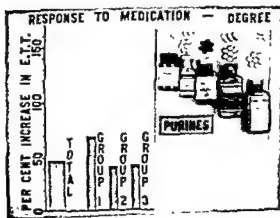
The efficacy of these preparations can be illustrated by comparing them with nitroglycerin (Plate 39, page 72). Administration of nitroglycerin before exercise enables patient, S W., to do over 75 percent more work than is otherwise possible. This response reaches its maximum in 3 minutes and is gone in 20 minutes.

The effect of Theobromine Sodium Acetate is equally striking, although somewhat less pronounced. Fifteen minutes after the administration of a capsule or a tablet, this patient can do 57 per cent more work than was possible without medication. This effect persists for about 3 hours.

The therapeutic action of the enteric coated tablet is more delayed and also more prolonged. The enteric coating prevents absorption for about 4 to 6 hours, but its therapeutic effect continues for almost 10 hours. Following its use, this patient is able to do about 50 per cent more work than was otherwise possible.



(Figure 34)

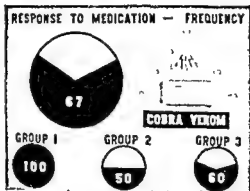


(Figure 35)

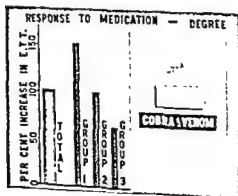
The purines are of value in about 45 per cent of the total number of patients (figs 34, 35), 85 per cent of those in group 1, but only 12 per cent in group 3. The average increase in exercise tolerance following the use of the purines is approximately 50 per cent.

# COBRA VENOM

The use of cobra venom as an analgesic deserves special mention. Many patients to whom the drug is given develop a marked decrease in attacks of pain in daily life and are able to do considerably more work under standardized conditions. Furthermore, this drug is of value in many patients who do not respond to other available medications (figs 41, 42).



(Figure 41)



(Figure 42)

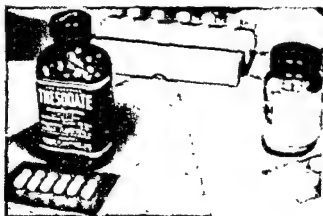
There are two drawbacks to its general use. First, the drug must be injected intramuscularly every day for at least a week before an effect is obtained, and it must be continued indefinitely at least twice weekly to maintain an effect. Many patients are unable to continue this form of treatment because of inconvenience and cost. The second drawback is that it acts solely as an analgesic. The lack of vasodilating action can be shown by electrocardiographic studies (Plate 42, page 72). If we compare the electrocardiogram with the patient standing at rest with that taken during an attack, we see the typical S-T deviation. Cobra venom causes no change in the electrocardiogram at rest. After exertion, however, although the patient does not experience pain, the electrocardiogram is still typical of angina.

Cobra venom is of value for symptomatic relief even though there is no basic cardiac improvement. In selected cases it may obviate the necessity for surgery.

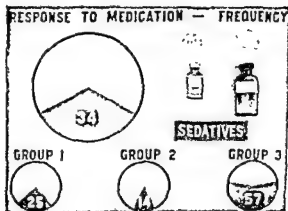


## SEDATIVES

The sedatives have a definite place in the treatment of angina pectoris, both alone and in combination with other drugs. Many such combinations are available on the market (fig 38).



(Figure 38)

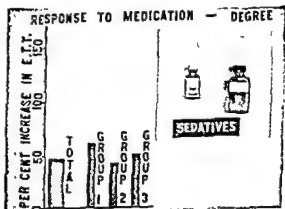


(Figure 39)

The beneficial results of the sedatives are probably due to a decrease in emotional activity which results in a decreased frequency of attacks. As many patients state "it makes the pain easier to bear". The sedatives most commonly used are the bromides and the barbiturates, especially phenobarbital.

The opiates are extremely valuable. Since they are habit forming, they are best reserved for acute exacerbations of the disease.

An increase in exercise tolerance following the use of these drugs is not common, but does occur in some patients who are helped by few other drugs (figs 39, 40).

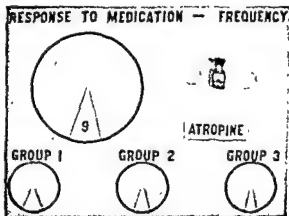


(Figure 40)



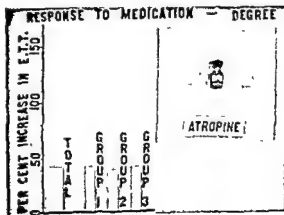
## THERAPY ACTING ON THE AUTONOMIC NERVOUS SYSTEM

Therapy which acts on the autonomic nervous system includes atropine, physostigmine, and carotid sinus stimulation. All these are of some value in angina.



(Figure 43)

Only a few patients respond to atropine, but this drug is of importance because it is of benefit to some persons in group 3 (figs 43-44).



(Figure 44)

Carotid sinus pressure and physostigmine, both of which stimulate the vagus nerve also have a beneficial effect in some patients.

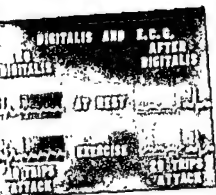


Figure 43—Digitalis may be injurious in angina pectoris

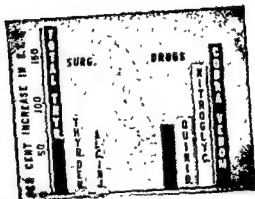


Plate 44—Comparative value of medical and surgical procedures



Figure 45—Methods of decreasing demand in angina pectoris



Plate 46—Methods of increasing supply angina pectoris



Figure 47—Symptomatic relief without

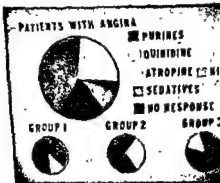


Plate 48—The "routine" treatment

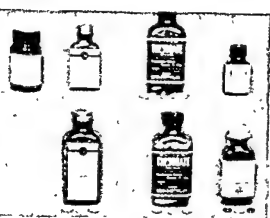


Plate 37—The most effective purines



Plate 38—Uncoated and enteric coated purines

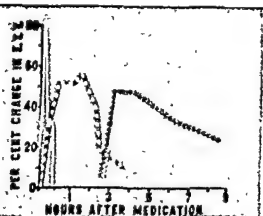


Plate 39—The value of theobromine sodium acetate



Plate 40—Enteric coated potassium iodide

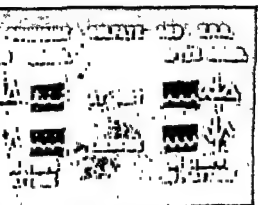


Plate 41—Value of quinidine sulphate in angina pectoris

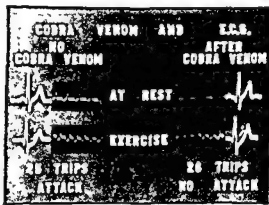


Plate 42—Symptomatic value of cobra venom

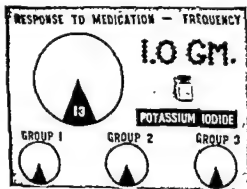
## IODIDES

The iodides are of undoubted value in those few cases of angina secondary to thyrotoxicosis or syphilis. The doses commonly used, however, have proven of little value in the usual case of angina pectoris. It frequently requires as much as 35 drops of the saturated solution to equal 1 cc or 1 gram of drug, hence 15 drops 3 times a day is really a small dose (fig 45)



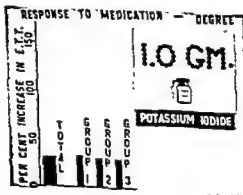
(Figure 45)

Larger doses, one gram 3 or 4 times daily, have been found to be of greater value in a few cases, especially those in Group 3 who are



(Figure 46)

unlikely to be helped by other medication. In order to avoid gastric distress, this is best given as an enteric coated tablet (figs 46-47), (Plate 40, page 72)



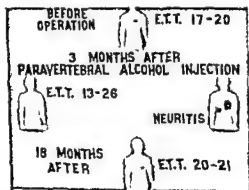
(Figure 47)



## PARAVERTEBRAL ALCOHOL INJECTION—THYROID DENERVATION

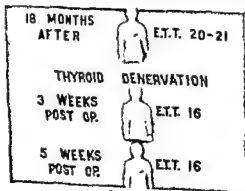
half refused operation when the risks and likelihood of benefit were explained to them. As a net result, surgery was performed in only seven per cent of the patients with angina who came to the hospital for treatment.

The results in patient R S who was incapacitated by angina pectoris for over 6 years illustrate the effect of surgery on the sympathetic nervous system (fig 50). His exercise tolerance was 17 to 20 trips, and his pain was experienced in the second interspace on the left and along the inner aspect of the left arm. After paravertebral alcohol



(Figure 50)

injection the severity of the attacks decreased strikingly. They were limited to a small area encircling the left wrist. His ability to work, however, was not increased. Simultaneously, he developed a severe neuritis which persisted for over a year. Before the neuritis subsided completely the original syndrome returned in its original location and severity. Eighteen months after (fig 51) because of continuation of his



(Figure 51)

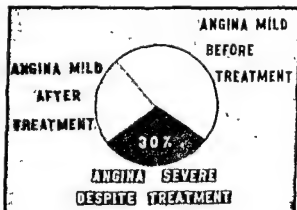


## DIGITALIS

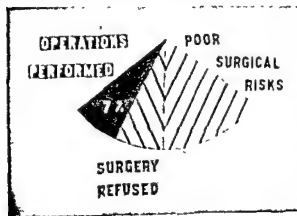
The digitalis bodies deserve special mention, for these drugs are frequently harmful to patients with angina pectoris. This can be shown objectively by electrocardiograms and exercise tolerance studies. For example, when no medication was given, patient M. L. developed an attack on performing 40 trips, and the electrocardiogram shows the typical S-T depression (Plate 43, page 73). When these studies were repeated after digitalization, the electrocardiogram taken at rest showed no striking changes. On exercising, however, the patient developed a severe attack after 28 trips. The electrocardiogram shows a marked depression of the S-T segment. This striking decrease in exercise tolerance was accompanied clinically by a corresponding increase in the frequency and severity of attacks in daily life.

## SURGERY

There are numerous reports in the literature on the surgical treatment of angina pectoris. Obviously, evaluation of the results of surgery is just as unreliable as the purely clinical evaluation of medical therapy. Experience at the Beth Israel Hospital indicates that in 46 per cent of patients with angina, the symptoms even without treatment are so mild that



(Figure 48)



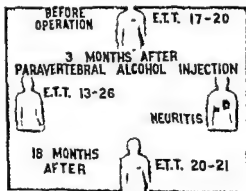
(Figure 49)

surgery is not indicated (fig. 48). In another 24 per cent, the response to medical treatment makes surgery unnecessary. This leaves 30 per cent of patients in whom the symptoms were severe despite therapy (fig. 49). Since angina pectoris is the result of an aging process, it is not surprising that one-half of these are poor surgical risks. Of the remainder,

## PARAVERTEBRAL ALCOHOL INJECTION—THYROID DENERVATION

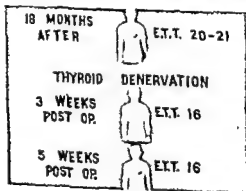
half refused operation when the risks and likelihood of benefit were explained to them. As a net result, surgery was performed in only seven per cent of the patients with angina who came to the hospital for treatment.

The results in patient R S who was incapacitated by angina pectoris for over 6 years illustrate the effect of surgery on the sympathetic nervous system (fig 50). His exercise tolerance was 17 to 20 trips, and his pain was experienced in the second interspace on the left and along the inner aspect of the left arm. After paravertebral alcohol



(Figure 50)

injection the severity of the attacks decreased strikingly. They were limited to a small area encircling the left wrist. His ability to work, however, was not increased. Simultaneously, he developed a severe neuritis which persisted for over a year. Before the neuritis subsided completely the original syndrome returned in its original location and severity. Eighteen months after (fig 51) because of continuation of his



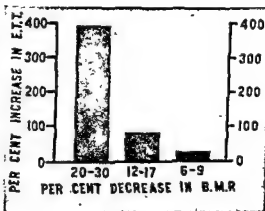
(Figure 51)

angina, thyroid denervation was performed. He was more comfortable after this operation. His exercise tolerance remained the same, but the pain was less severe and was limited to the left arm. Five weeks later, however, the symptoms returned.

Sympathetic nerve surgery, therefore, results in symptomatic relief without any increase in ability to work.

The most striking results which we have observed were obtained by Total Thyroidectomy (fig 52). This procedure lowers the metabolism and thereby decreases the work of the heart. Those patients whose basal metabolic rates were decreased by 20 to 30 per cent showed an average increase in exercise tolerance of nearly 400 per cent. They were also practically free from attacks in daily life.

Patients who showed a moderate fall in basal metabolism showed proportional improvement, while those who showed little change in metabolism had no clinical improvement and no appreciable increase in exercise tolerance.



(Figure 52)

We have seen that few patients require surgery. In suitable cases, however, the beneficial response to total thyroidectomy may be marked and the untoward effects negligible.

The comparative effect of medical and surgical therapy can be illustrated as follows (Plate 44, page 73). Following the use of the purines, patients in Group I show an increase in exercise tolerance of 70 per cent. The use of quinidine results in a 75 per cent increase in exercise tolerance. Nitroglycerin causes an increase of 120 per cent. Cobra venom enables patients to do about 150 per cent more work. Although the patient may be more comfortable following paravertebral alcohol injection, there is usually no appreciable increase in ability to work. The same is true following denervation of the thyroid gland. After total thyroidectomy on the other hand, the average increase in exercise tolerance of all patients studied was 180 per cent.

## THE ROUTINE TREATMENT OF ANGINA PECTORIS

Treatment must be individualized. Specific emotional or exertional factors responsible for attacks can be eliminated in many cases. In others hyperthyroidism, anemia or arrhythmias may be corrected with benefit. In most patients, medication is necessary. As a result of measuring the value of 70 different therapeutic agents, it is possible to present a practical plan of therapy using those preparations most likely to be of value in the largest number of cases (Plate 48, page 73)

The punnes, if given in adequate doses, are most likely to be of benefit. These will help about 43 per cent of all patients, 85 per cent of Group 1, 50 per cent of Group 2, but only 12 per cent of Group 3. If medication is of value, it will be evidenced within a week by complete or almost complete disappearance of attacks in daily life. Any improvement short of this is not due to the medication used. If no satisfactory response is obtained, it is advisable to administer quinidine sulfate as the next drug most likely to be of benefit. Sixty per cent of all patients are helped by either the punnes or quinidine. This includes all patients in Group 1, 70 per cent of Group 2, but only 24 per cent of Group 3. The treatment of the remaining 40 per cent of patients, especially those in Group 3, is the present problem and recent studies have concentrated on a search for therapeutic agents which will help this group. Atropine sulfate, though not as valuable as the punnes or quinidine, may help 10 per cent of such patients in Groups 2 and 3. The sedatives, phenobarbital or codeine sulphate, will help other patients in Group 3 and, of course, are of value as an adjunct to other therapy in all patients. There remains about 20 per cent of patients, two-thirds of whom are in Group 3 who respond to none of these medications.

In patients with severe angina, it is advisable to use combinations of medication. Such treatment should begin with a period of complete bed rest. Adequate sedatives, either barbiturates or opiates, should be given. This may be combined with small frequent doses of nitroglycerin 1/400 every hour. In some instances, it may be advisable to give an active punne in addition, and, if necessary, quinidine sulphate.

This regime will result, usually, in complete disappearance of pain, unless there has been a recent coronary occlusion or there is a strong emotional element. Cobra venom is advisable if the symptoms return when the patient is allowed up and about again. If this fails to give relief, surgery should be considered, total thyroidectomy in suitable cases, sympathetic nerve surgery in others.





In summary, since angina pectoris occurs when the Supply of blood is inadequate for the Demands of the heart, treatment may take 3 general forms.

The first consists of **decreasing the Demand** for blood by rest, sedatives, or if necessary, decreasing the metabolic needs of the body by total thyroidectomy (Plate 45, page 73).

The second method of treatment consists of **increasing the supply** of blood by the use of drugs such as nitroglycerin, the purines, and quinidine sulphate (Plate 46, page 73)

The third type of therapy (Cobra Venom and Sympathetic Surgery) should be used only where it is impossible to readjust the balance between Supply and Demand by the above methods (plate 47, page 73) Here, the underlying physiological mechanism responsible for the attacks is not altered, but the procedure **interrupts the sensory nerves** so that pain is not experienced.

The aims of treatment in angina pectoris are First, relief of discomfort, Second, *prolongation of life and prevention of myocardial infarction*, and, Third, economic rehabilitation if possible, or at least prevention of cardiac invalidism The plan of treatment just outlined, together with a thorough understanding of the patient and his condition, goes a long way towards fulfilling these aims

